REMARKS

The applicants appreciate the Examiner's thorough examination of the application and request reexamination and reconsideration of the application in view of the following remarks.

The Examiner rejects claims 1-10, 13-24 and 27 under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. No. 6,554,819 to *Reich*. The Examiner also rejects claims 11, 12, 25 and 26 under 35 U.S.C. §103(a) as being unpatentable over *Reich* in view of *Doty et al.*, Effect of Increased Renal Venous Pressure on Renal Function.

The applicants recognized that renal dysfunction is associated with the use of radiographic contrast media, and recognized the need to reduce the incidence and severity of contrast associated nephropathy. See e.g. applicants' specification at page 5, lines 8-10 and page 7, lines 17-19.

The applicants also recognized that contrast agents affect the target organ in proportion to the concentration of active chemical agent in blood plasma that flows through the organ – e.g. a kidney – and the duration of exposure. Kidneys are damaged primarily by exposure to high concentrations of contrast in blood. See e.g. applicants' specification at page 9, lines 17-23 and page 13, lines 4-5.

The applicants further recognized that elevated renal vein pressure often exhibits diminished renal function and reduced renal blood flow, that such diminished renal function and reduced venal blood flow would be beneficial to protect the kidney(s) during times of peak exposure to a contrast agent, and that one way to effect elevated renal vein pressure is by

creating a removable obstruction of the renal vein. See e.g. the applicants' specification at page 17, lines 10-27 and at page 18, lines 1-4.

These concepts and more are more fully set forth in the applicants' specification.

In summary, in accordance with one embodiment of the subject invention, the applicants have disclosed prevention of radiocontrast nephropathy by increasing renal vein pressure in at least one kidney.

At least partially occluding at least one renal vein (through which blood flows from the kidney) of a patient, and increasing a renal vein blood pressure, as claimed by the applicant, serves to reduce renal function.

This is beneficial especially during the peak administration of the contrast agent when its concentration in the blood is the highest. Thereafter, when most of the contrast agent is redistributed, the concentration of contrast is no longer high, and the kidney(s) alone can clear contrast from the blood. See e.g. the applicants' specification at page 30, lines 1-13 and page 29, lines 17-20, and page 10, lines 8-11. Thus:

> The kidney remains protected by 'hibernation' for the duration of high concentration that is expected to last several hours while the contrast is redistributed from vascular compartment to the total body distribution volume.

See e.g. the applicants' specification at page 3, lines 9-14.

The applicants' claim 1 recites a method for protecting a kidney in a mammalian patient from an insult comprising: at least partially occluding at least one renal vein of the patient; elevating a renal vein blood pressure, and reducing the renal vein blood pressure from the elevated blood pressure.

The applicants' independent claim 14 recites a method for minimizing radiocontrast nephropathy in a mammalian patient comprising: at least partially occluding at least one renal vein of the patient, and elevating a renal vein blood pressure during a period coinciding with an injection of contrast in blood of the patient.

The applicants invention claimed in independent claims 1 and 14 is in sharp contrast to *Reich*.

In contrast to the applicants' claimed invention, *Reich* fails to disclose partially occluding at least one renal vein of the patient. It is well established, and would be recognized by those skilled in the art, that the renal vein carries blood from the kidney, to the IVC and subsequently to the heart. See also e.g. applicants' specification at page 23, lines 22-24 and Fig. 2. (Renal arteries provide blood flow to the kidney(s) (and would include contrast agent)).

In further contrast to the applicants' claimed invention, *Reich* fails to disclose elevating a renal vein blood pressure, at least as a consequence of failing to occlude a renal vein in the first instance.

In stark contrast to the applicants' more natural, miniminally invasive method and system, *Reich* discloses a highly complex and unduly invasive system to: first, divert blood which is flowing (containing contrast) to the organ/kidney (so that the blood flow with contrast does not reach the organ/kidney in the first instance); second, filter out the contrast agent using a machine; third, adding water to the blood to replace the contrast removed; and fourth, reinfusing the blood and water into the patient.

Reich thus specifically teaches blocking blood flow – which include contrast agent – to the kidney, whether at the coronary sinus or from a "vein" to the patient's kidneys as disclosed

by *Reich* at column 5, lines 18-21. The blood and contrast agent are blocked from reaching the kidney and bypassed to a filtration machine outside the patient's body in order to filter out the contrast solution. See also e.g. *Reich* column 2, lines 36-42. Water is then added to the blood to replace the contrast solution and reinfused into the patient. See *Reich* column 3, lines 4-7.

Reich cryptically posits that his method may block flow of contrast in veins draining the organ (such as the kidney, see e.g. *Reich* at column 5, lines 15-16). This is clearly a result of *Reich* preventing the contrast from getting to the kidney in the first instance, however, and not a result of blocking a renal vein to partially occlude flow from the kidney(s).

Moreover, it would follow that blocking fluid to the kidney(s) would decrease, not increase, renal pressure.

These teachings by *Reich* in fact make it clear that the structure, function, and principle of *Reich* is starkly different than the applicant's claimed invention.

Accordingly, it is clear that *Reich* fails to teach the applicants' claimed invention or the elements of the applicants' independent claims 1 and 14, and the applicants therefore submit that claims 1 and 14 are in condition for allowance. Claims 2-13 ultimately depend from claim 1, and claims 15-27 ultimately depend from claim 45. Accordingly, these dependent claims are in condition for allowance over *Reich (*and/or *Reich* in combination with *Doty et al.)* for at least these same reasons.

CONCLUSION

The applicants submit that in addition to claims 21-44, claims 1-20 and claims 45-61 and 64-66 are in condition for allowance.

Each of the Examiner's rejections has been addressed or traversed. Accordingly, it is respectfully submitted that the application is in condition for allowance. Early and favorable action is respectfully requested.

If for any reason this Response is found to be incomplete, or if at any time it appears that a telephone conference with counsel would help advance prosecution, please telephone the undersigned or his associates, collect in Waltham, Massachusetts at (781) 890-5678.

Respectfully submitted,

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